



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2020-N-1806]

Fit for Use Pilot Program Invitation for the Clinical Data Interchange Standards

Consortium for Standard for Exchange of Nonclinical Data Implementation Guide

Developmental and Reproductive Toxicology: Version 1.1

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing that it intends to conduct a Fit for Use (FFU) pilot program to test the processing and analysis of nonclinical study data provided electronically for the Clinical Data Interchange Standards Consortium (CDISC) for Standard for Exchange of Nonclinical Data (SEND) Implementation Guide (IG): Developmental and Reproductive Toxicology v1.1 (SEND-DART). The Agency's Center for Drug Evaluation and Research (CDER) will test the processing and analysis of nonclinical study data provided electronically in SEND-DART format. FDA is inviting individual firms that wish to participate in this pilot program to submit participation requests via email or in writing.

DATES: To be considered for participation in the pilot program, submit electronic or written requests by February 26, 2021. See the ADDRESSES section for participation request instructions.

ADDRESSES: Submit electronic requests to participate in the pilot and comments regarding this pilot project to Docket No. FDA-2020-N-1806 at <https://www.regulations.gov> . Submit

written requests to participate in the pilot and comments regarding the pilot to Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. The <https://www.regulations.gov> electronic filing system will accept comments until 11:59 p.m. Eastern Time by February 26, 2021. Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are postmarked or the delivery service acceptance receipt is on or before that date.

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in “Instructions.”

Instructions: All submissions received must include the Docket No. FDA-2020-N-1806 for “Fit for Use Pilot Program Invitation for the Clinical Data Interchange Standards Consortium for Standard for Exchange of Nonclinical Data Implementation Guide: Developmental and Reproductive Toxicology v1.1.” Received comments will be placed in the docket and, except for those submitted as “Confidential Submissions,” publicly viewable at <https://www.regulations.gov> or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240-402-7500.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states “THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.” The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made

publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as “confidential.”

Any information marked as “confidential” will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA’s posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: <https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the “Search” box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240-402-7500.

FOR FURTHER INFORMATION CONTACT: Jesse Anderson, Office of Computational Science, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 21, Rm. 1553, Silver Spring, MD 20993-0002, 301-348-1816, Jesse.Anderson@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background

Data Standards help FDA receive, process, review and archive submission data more efficiently and effectively. Study data standards describe a standard way to exchange clinical and nonclinical research data between computer systems. These standards provide a consistent general framework for organizing study data, including templates for datasets, standard names

for variables, and a standard way of doing calculations with common variables. Study data standards are required for study data submitted to FDA's CDER per the published guidance¹.

CDISC is an open, multidisciplinary, nonprofit organization that has established worldwide industry standards to support the electronic acquisition and submission of study data and metadata for medical and biopharmaceutical product development². CDISC is currently facilitating and testing the extension of the SEND-DART standard for nonclinical toxicology data.

CDER completed a pilot project evaluating SEND 3.1 using SEND-formatted sample toxicology datasets. Phase 1 of the pilot supported the development of a SEND Implementation Guide (SENDIG) describing the process for formatting data from single and repeat-dose animal toxicity and carcinogenicity studies for submission purposes. During Phase 2 of the pilot, CDER evaluated submission of SEND formatted datasets and evaluated data validation and analysis tools capabilities. The outcomes of this pilot resulted in improvements to the SENDIG 3.1.³

Based on published guidance⁴ studies initiated after December 17, 2016, must be submitted with data formatted in accordance with the data standards listed in the FDA Data Standards Catalog for new drug applications (NDAs), biologics license applications (BLAs), and abbreviated new drug applications (ANDAs). For investigational new drug applications (INDs), the requirement⁵ applies to studies initiated after December 17, 2017. Different versions of SENDIGs are on the Data Standards Catalog, and the submission of SEND nonclinical datasets

¹ See the guidance "Providing Regulatory Submissions in Electronic Format-Standardized Study Data; Guidance for Industry" at <https://www.fda.gov/media/82716/download>.

² See the CDISC website at <https://www.cdisc.org>.

³ The updated guide can be found at <https://www.cdisc.org>. FDA has verified the website address, but the Agency is not responsible for any subsequent changes to the website address after this document publishes in the *Federal Register*.

⁴ See the Technical Rejection Criteria for Study Data at <https://www.fda.gov/media/100743/download>.

⁵ See footnote 4.

is expected to continue to increase in the future. This pilot will evaluate the compliance of sample SEND-DART datasets submitted to CDER. As part of this evaluation and in anticipation of FDA receiving datasets for regulatory review, the CDISC SEND team, in collaboration with CDER and available pilot participants, will update the SENDIG-DART as needed to include specific data elements and terms.

II. Project Participation

CDER is seeking a maximum of five participants in this pilot. The Center will use its discretion in choosing participants based on the completeness of the submission per the guidelines below. CDER requests participants to submit a nonclinical study package containing the materials:

- SEND-DART v1.1 datasets;
- final related study report containing individual animal data and summary tables⁶ (PDF Format);
- nonclinical Study Data Reviewers Guide⁷;
- define.xml (v2.0)⁸; and
- sample standardization study protocol.

CDER will prioritize nonclinical packages that contain Embryo-Fetal Development (EFD) Toxicity studies (using pre-bred females only) that contain data that is consistent with SEND-DART v1.1. Therefore, the studies that meet as many of the following use cases as possible will be the most sought out as participants in this pilot:

⁶ See the FDA Study Data Resources web page, available at <https://www.fda.gov/ForIndustry/DataStandards/StudyDataStandards/default.htm>.

⁷ See the PhUSE Wiki web page, available at https://www.phusewiki.org/wiki/index.php?title=Nonclinical_Study_Data_Reviewers_Guide.

⁸ See Footnote 6.

- small animals (rodents, rabbits), pre-bred females, treatment period during implanted embryo's major organogenesis period;
- material toxicity endpoints (minimum CL, BW, FW, DS);
- caesarean section endpoints in PY, IC, FM, FX (pregnancy, Corpora Lutea, implantations, resorptions, fetal viability, fetal sex and body weights, fetal morphology);
- toxicokinetic females to illustrate in Trial Design and pregnancy results (PC, PP domains optional);
- LB domain optional since not routine in EFD Toxicity study;
- MA optional (if gross observations scheduled, may not be in preliminary EFD study);
- gravid uterine weights (OM domain) for deriving gravid uterus adjusted body weight; and
- pregnant, non-pregnant, toxicokinetic females to illustrate in Trial Design and pregnancy results (PC, PP domains optional)

Please indicate in your request for participation the extent to which your submission will meet the above listed criteria. Please also indicate whether you are willing to share anonymized data with the CDISC FFU team.

This pilot is intended to inform of the readiness of the SEND-DART standard and support improvements to the SEND-DART that will benefit FDA and submitters. Pilot participants commit to publicly share lessons learned with the CDISC SEND team to ensure that the CDISC SEND standard is improved for the community. Participants may redact any sensitive information as needed to enable sharing FDA feedback with the CDISC SEND team.

III. Requests for Participation

Requests to participate in the SEND-DART FFU pilot are to be identified with the Docket No. FDA-2020-N-1806. Interested persons should include the following information in

the request: contact name, contact phone number, email address, name of the sponsor, and address, as well as the description of the criteria met, addressing each of the items in the Project participation section.

Once requests for participation are received CDER will contact interested sponsors to discuss the pilot project and clarify requirements and expectations. The elapsed time duration of the pilot is expected to be approximately 9 months but may be extended as needed.

Dated: October 16, 2020.

Lauren K. Roth,

Acting Principal Associate Commissioner for Policy.

[FR Doc. 2020-23393 Filed: 10/21/2020 8:45 am; Publication Date: 10/22/2020]